62 YO F presents with painful, red left eye

- Patient reports she has a contact lens stuck in her eye and needs help removing it.
- Went to urgent care to have CTL remove—no success.
- Referred to OD.
- Oxidized copper sulfite and patched eye.
- Pain reported as “worse than childbirth.”

### Prelims

**VA (cc):** 20/30 OD, 20/400 OS

**IOP deferred**

**Pertinent Findings (OS)**

- Conj: 2+ diffuse injection, subconj. heme-temp, mod limbal staining – nasal
- K: large geographic epithelial defect. Only ½ of K epithelial intact. No underlying haze or stromal edema. Grade 1-2 Dfolds
- A/C: Mild cell

### What is Pain?

*“an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”*

### Visual Analog Scale (VAS)

![Visual Analog Scale](https://www.dovepress.com/wet-transepithelial-phototherapeutic-keratectomy-in-the-management-of-peer-reviewed-article-OPTH)

1. The International Association for the Study of Pain (IASP)
Pain Management

- Do we manage pain?
- Tell her to sleep it off?
- Go drink a six pack?

If we are going to address PAIN, we need to manage PAIN!

Mechanisms of Pain and Analgesia

- Nociceptors, specialized pain endings
- Activated by trauma and chemical substances (Prostaglandins) released in response to injury
- Pain signals are conveyed to central nervous system (CNS)

Mechanisms of Pain and Analgesia

- COX-1 “housekeeping enzyme”
  - It is widely distributed in most tissues
  - Protects: gastric mucosa, kidney function maintenance and protection, regulating platelet aggregation

- COX-2
  - Initiation and maintenance of the inflammation process
  - Minor roles for preventing platelet aggregation (clustering)


Classification of Analgesics

- "Peripheral" acting agents
  - OTC products, non-narcotic analgesics
- "Central" acting agents
  - Controlled substances
- Anesthetics—never prescribed
- Adjuvants (e.g., caffeine)

Ocular Pharmacokinetics Review

Ocular (Local) Drug Fate

25% of topical drug concentration is lost from evaporation on installation!

Pharmacokinetics (cont.)

Metabolism
- Drug Binding
- Ciliary Body
  - Major ocular source of metabolizing enzymes
- Prodrugs
  - Must be metabolized to be active
Elimination
- Retinal Vessels -> Uveal Vessels -> Direct outflow pathway

Corneal Transmissibility
Drug at Equilibrium
Tear film buffers drug to a pH of 7.4
pH of tear film 7.4
Drop pH is 6
Drug at Equilibrium
Tear film buffers drug to a pH of 7.4
pH of tear film 7.4
Ionized portion (water soluble)
The non-ionized (lipid soluble) portion will penetrate the epithelium

Drug reorganizes to Equilibrium
Tear film buffers drug to a pH of 7.4
Drug reorganizes to Equilibrium
Tear film buffers drug to a pH of 7.4

Drug Absorption FYIs
- BAK and drug penetration
- Corneal CXL and drug penetration
  - Corneal cross-linking with ultraviolet-A and riboflavin results in a statistically significant reduction in corneal permeability.
  - Diseases such as diabetes can result in increased corneal cross-linking through the sustained elevation of glucose levels.

**Drug Absorption**

- Most ocular drugs are formulated as weak bases because of more non-ionized portions of the drug reaching the aqueous humor
  - Better penetration
  - Better bioavailability

**Lipid Soluble (Lipophilic) = Non-ionized**

**Drug Absorption**

**Efficacy Versus Potency**

- Topical dexamethasone alcohol 0.1% is known to have a six-fold higher potency and double the half-life of topical prednisolone acetate 1%
- Pred Acetate attained a peak aqueous concentration that was more than 21 to 36 times higher (than Dex) and persisted with a detectable drug aqueous concentration after 24 hours (Dex was undetectable)


**Local Anesthetics**

- 800 A.D. First documented use
- Benzoic acid ester
- Led to synthesis of procaine 1905, then lidocaine 1940’s for WWII

**Local Anesthetics**

- • Mechanism of Action
  - Inhibits excitation of nerve endings or by blocking conduction in peripheral nerves.
  - Esters metabolized in the plasma
  - Amides metabolized in the liver

**Local Anesthetics**

- Injectables
  - Lidocaine (xylocaine) 1%
  - with or without epinephrine (0.5mL to 1mL)
  - Bupivacaine

**Local Anesthetics**

- Topicals
  - Esters
  - Tetracaine
  - Benzocaine
  - w/fluoresceine or fluorescamine
  - Proparacaine
  - Amide
  - Lidocaine (Akten)
Local Anesthetics

Topical Anesthetics
- Esters
  • Tetracaine
  • Benoxinate
    - w/fluorescein or fluorexon
  • Proparacaine
- Amide
  • Lidocaine (Akten)

All have rapid onset of anesthesia beginning within 13-30 second
Duration: 15-20mins


Local Anesthetics
Contraindications
- Known hypersensitivity

Local Anesthetics
Side Effects
- Allergy
  - Allergic reactions to local anesthetics occur almost exclusively to those with ESTER linkage (topicals, except Akten)
- Literature reports demonstrate that cross-sensitivity reactions are rare between proparacaine (Ophthetic®, Alcaine®), an ester, and other ester anesthetics.
- Stinging
- Burning
- Conjunctival Redness
- Corneal Toxicity


Topical anesthetics and Corneal Toxicity
- Shown to be toxic to the cornea in Laboratory Experiments:
  - Direct toxicity to cytoskeletal structures and cellular function
  - Indirect toxicity causing the loss of epithelial microvilli, which leads to tear film instability, desiccation, and inhibition of reepithelialization.1, 1
  - Blocking the natural tear production reflex to noxious stimuli causes tear production and blinking rate to decrease.1
  - Thought to increase corneal permeability and swelling, may result in a loss of corneal transparency.1
  - Increased epithelial sloughing rates have also been demonstrated, suggesting decreased adherence of the epithelial cells and delayed healing.1


62 YO F presents with painful, red left eye
- The patient was dispensed Tetracaine by the NP she saw at Urgent Care facility.

12-month, prospective, double-blind, randomized trial of PF tetracaine hydrochloride 1% vs. PF saline, n=116 (UC Davis)
- Applied q30 mins while awake for 24 hrs.
- *1000mg APAP PO QID
- Results: No complications in the 59 patients receiving tetracaine.
- No difference in K healing
- No clinical difference in pain scores from each group
- Perceived drug effectiveness: significantly higher for tetracaine group
- Large corneal abrasions were excluded

ORIGINAL CONTRIBUTION
Topical Tetracaine Used for 24 Hours Is Safe and Rated Highly Effective by Patients for the Treatment of Pain Caused by Corneal Abrasions: A Double-blind, Randomized Clinical Trial
Nati Waldman, MD, FACOM, Ian K. Denis, and Pierre Hébert, DSc;
- 12-month, prospective, double-blind, randomized trial of PF tetracaine hydrochloride 1% vs. PF saline, n=116 (UC Davis)
- Applied q30 mins while awake for 24 hrs. *1000mg APAP PO QID
- Results: No complications in the 59 patients receiving tetracaine.
- No difference in K healing
- No clinical difference in pains scores from each group
- Perceived drug effectiveness: significantly higher for tetracaine group
- Large corneal abrasions were excluded
Weaknesses

Lay person could have examined the patient:

- “The ability to detect the complications was limited by the physicians performing the follow-up, not all patients were examined by an emergency specialist or ophthalmologist, and it is possible that complications were missed or developed later.”

Support for anesthetics

- Concerns regarding human complications are based on case reports describing the unsupervised, prolonged use of topical anesthetics.
- Most reports are >25 yrs old
- Support use of anesthetics with preservatives
- Anesthetics for pain control after PRK surgery, 3,4
- No delayed healing at 72 hours.

Topical NSAIDs

- Primary indications
  - Post-Op Cataract sx inflammation
  - Indicated for corneal pain
  - Refractive surgery
  - Corneal trauma
  - Post Argon Trabeculoplasty inflammation
  - CME

  - Reduces levels of both prostaglandins and leukotrienes
  - Reduces corneal pain by reducing PGE2 levels in cornea

Topical NSAIDs

- Diclofenac sodium
- Ketorolac
- Bromfenac
- Nepafenac
Diclofenac 0.1%

- Voltaren (discontinued)
- QID dosing
- Generic Cheap: ~$9/5mL
- Generic version largely reported in literature for corneal melts

Ketorolac Tromethamine

- Acular 0.5%
- QID dosing
- Generic $14

Nepafenac

- Suspension must shake
- Reversal: 0.1%
  - TD dosing
  - 1500
- Ilevro 0.3%
  - Qd dosing
  - $260
- Nepafenac 0.1%, bromfenac 0.09%, and ketorolac 0.45% were compared to determine which most effectively reduced prostaglandin E₂ (PGE₂) following surgery. PGE₂ concentrations were significantly lowest in the ketorolac group, followed by the bromfenac and nepafenac groups, respectively.
- The maximal absolute drop in corneal sensitivity as measured by pressure thresholds was greatest for diclofenac [28.6 mm], followed by ketorolac [21.1 mm], bromfenac [16.9 mm] and nepafenac [16.4 mm].
- No statistical difference observed between nepafenac 0.1% and ketorolac 0.4% in postoperative pain scores.

Corneal PAIN relief

- No significant difference
- Nepafenac: 0.1%, bromfenac: 0.09%, and ketorolac: 0.45% were compared to determine which most effectively reduced prostaglandin E₂ (PGE₂) following surgery. PGE₂ concentrations were significantly lowest in the ketorolac group, followed by the bromfenac and nepafenac groups, respectively.
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- No statistical difference observed between nepafenac 0.1% and ketorolac 0.4% in postoperative pain scores.

Bromfenac

- Generic Bromfenac 0.09%
- Qd dosing
- S80
- Bromfenac 0.07% (Prolensa)
  - Qd dosing
  - Lower pH allows 0.07% concentration to perform as well as the generic 0.09%.
  - Highly lipophilic -> high corneal permeable. Almost structurally similar to amfenac.
- Bromfenac 0.075% (BromSite)
  - BID dosing
  - Duratec delivery is thought to extend the drugs residence on the ocular surface
- Bromfenac 0.09% (ProIntra)
  - TD dosing
  - $250

Corneal Epithelial Wound Healing w/NSAIDs

- No significant difference
- Nepafenac: 0.1%, ketorolac: 0.4%, bromfenac: 0.09%
- Average time for healing was 4-days (post-PRK)
- Less overall irritation with nepafenac and bromfenac
Case 1 management

- In-office
  - polymyxin B/Bacitracin ung in-office and pressure patched

- Prescribed
  - Polymyxin B/Bacitracin ung QID, Bromsite BID
  - Alternate Oral Tylenol and Ibuprofen, not to exceed 4000mg daily
  - Suggested cool compresses prn

Case II

71 YO M with painful right eye.

- "so painful I could not sleep last night."
- Marked swelling and moderate ecchymosis above the right lacrimal sac.
- This area was very hard and ridged to the touch.

71 YO M with painful right eye.

- Dx
  - Dacryocystitis
  - h/o nasolacrimal tract issues, managed by ENT.

71 YO M with painful right eye.

- Health Hx:
  - DK, HCL, CAD, HTN, A-fib
- Meds
  - Amlodipine Besylate, Atorvastatin, Finasteride, Glipizide, HCTZ/Lisinopril, Metoprolol, Warfarin
- Allergies
  - Rocephin (3rd Gen Cephlosporin)

71 YO M with painful right eye.

- Management
  - Pain management
    - Vicodin Hydrocodone 5mg/Acetaminophen 325mg QID x 3d
  - Anti Inflammatory
    - Celebrex 300mg PO bid
  - Antibiotics
    - Vigamox TID QD
  - Monitor
Oral Agents

COX inhibition
- COX-1 inhibition → GI side effects
- COX-2 inhibition → Cardio side effects

Goal:
Selective COX-2 inhibitors, NOT specific COX-2 and still maintain some degree of COX-1 inhibition.

General consensus
- The advantages of COX-2 inhibitors
  - better dosing
  - limited GI toxicity
  - patient acceptability
- The COX-2 inhibitors may in some cases be given to patients who have a history of NSAID intolerance, GI sensitivity, GI ulceration, or renal and liver disease.

Non-narcotic Analgesics

NSAIDs
- Salicylates
  - Aspirin (Acetylsalicylic Acid, ASA)
- Non-Salicylates
  - Ibuprofen
  - Diclofenac
  - Celecoxib
  - Meloxicam
  - Naproxen
  - Naproxen sodium


Aspirin

- MA: non selective COX inhibitor, decreases COX1
- Adult dosage is 325-650mg q4h (with food)
- Main SE:
  - GI disturbances
  - Increased risk of allergic reaction in Asthmatics
  - Hemorrhage
  - Increased risk of MI and stroke.
  - Reye’s syndrome
  - Antiinflammation effect of 1 wk
- Preg C

FYL –

COX1 helps protect GI

Non-Salicylates

ibuprofen

- MA: non selective COX inhibitor
- Adult dosage
  - Analgesic 200-400mg q4-6h
  - Anti-inflammatory 600-800mg q4-6h
- Main SE:
  - GI disturbances
  - Hemorrhage
  - Reye’s syndrome
  - Antiinflammation effect of 1 wk

Non-OTC NSAIDs

- Motrin
- Ketoprofen
- Indomethacin
- Celecoxib
- Diclofenac
- Meloxicam
- rofecoxib

- Non-selective COX 1 /COX 2 inhibitors

celecoxib (Celebrex)

- MA: COX-2 specific inhibitor
- Adult dosage
  - Analgesic 200mg BID
- Advantages
  - Better for patients with GI issues
  - BID dosing
  - Better for long term pain management vs acute pain

Diclofenac sodium

- MA: COX 1 and 2 selective inhibitor
- Adult dosage
  - Delayed and Extended release
  - Analgesic 50mg BID-QID
- Advantages
  - Better for patients with GI issues
  - BID dosing
Meloxicam (Mobic)

- MA: COX-2 selective, but non-specific COX inhibitor
- Adult dosage
  - Analgesic: 7.5 to 15mg QD
- Benefits
  - Rare GI and CV side effects
  - Once a day dosing

Rofecoxib (Vioxx)

- MA: COX-2 selective, but non-specific COX inhibitor
- Adult dosage
  - Analgesic: 7.5 to 15mg QD
- Benefits
  - Rare GI and CV side effects
  - Once a day dosing

Remember Vioxx?

- Aka rofecoxib
- COX-2 selective NSAID
- VIGOR Study: The study showed that patients taking Vioxx had fewer stomach ulcers and bleeding than patients taking naproxen, another NSAID, however, the study also showed a greater number of heart attacks in patients taking Vioxx.
- Merck removed in 2004

Naproxen Sodium

- MA: COX-2 selective, but non-specific COX inhibitor
- Adult dosage
  - Analgesic: 7.5 to 15mg QD
- Thought by many to be safer than ibuprofen as far as cardiovascular
- "Many investigators and a lot of writing" hold naproxen to be safer than ibuprofen in terms of CV risk, perhaps because they perceive naproxen as primarily COX-1 selective, ”but in fact that’s not true.”

Choice of NSAID

- Clinical experience
- Patient convenience or preference
- Past history of favorable analgesic use
- Side effects
- Cost

NSAID Contraindications

- Active upper GI disease
- Bleeding disorders
- Following invasive surgery
- Chronic renal disease
- Pregnancy
- More than 3 alcoholic drinks daily
- Diabetics?
Displaced Protein Binding

- Protein-bound drugs are inactive pharmacologically.
- Administration of more than one drug bound to the same plasma protein binding site can cause either drug to be displaced from its binding site.
- NSAIDS = oral hypoglycemic.

Alcohol and NSAIDs

- Chronic alcohol consumption lowers albumin concentration.
- NSAIDs bind to albumin, so if albumin is not readily available to bind to drug, even a normal dose may cause toxicity.

Concomitant use of Ibuprofen and Aspirin

- Ex.
  - Patient on low-dose ASA (81mg)
  - In need of pain management
- Ibuprofen can interfere with anti-platelet effect of low-dose ASA.
  - Consider dosing Ibuprofen 30 mins after low dose aspirin
  - Dose Ibuprofen 8 hours before low dose aspirin

Acetaminophen (APAP)
Pharmacology

- Analgesic mechanism is unclear
- Activity in CNS?
- Analgesic effect is comparable to ASA except in inflammatory conditions
- APAP DOES NOT
  - inhibit platelet aggregation
  - affect prothrombin time
  - produce GI discomfort.

Clinical uses

- When NSAID therapy is contraindicated
  - Active upper GI disease, pregnancy, bleeding disorders, kidney disorder, NSAID allergy
- Children and adolescence

Commercial Formulations

- Approximately 100 single-entity products available
- Formulations
  - Suppository, chewable, tablet, capsule, elixir, liquid, solution
- All OTC as a single entity

Adult Dosage

- 325-650 mg q4-6h
- 1000 mg tid or qid
- No need to take with food
- Do not exceed 4 grams daily

Side Effects

- Liver damage in chronic alcoholics with pre-existing liver damage
- Liver toxicity in overdose (10-15 grams)

Narcotic (OPIOID) Analgesics
Narcotic (OPIOID) Analgesics

Definitions

- **Opioids**
  - Any drug which binds to the opioid receptors in the CNS and antagonized by Naloxone. They may be: Natural, Synthetic and Semi-synthetic.

- **Opiates**
  - Drugs derived from opium - Natural or semi-synthetic.

- **Narcotics**
  - Drugs derived from opium or opium-like compounds, with potent analgesic effects associated with significant alteration of mood and behavior, and with the potential for dependence and tolerance following repeated administration.

Opioids Pharmacology

- **Mu receptor agonists**
- **Central Acting**
  - Opioid receptors in the brain
  - Limit sensation of pain and its emotional response
  - **You don’t care!!**

Clinical uses

- May be safer for patients with contraindications to NSAIDs
- Adding a peripherally-acting analgesic provides additive or synergistic effects
- **No ceiling effect**
  - Can always increase the dose
  - Dose-liming component e.g. acetaminophen

What about the Opioid Crisis?

- "The side effect is, you don’t care what it costs."

Most Ophthalmologists wrote 10 opioid Rxs or fewer annually
Mean supply of 5 days
Are eyecare providers part of the problem?

Morphine
- The gold standard opioid
- Side effects and abuse potential limit outpatient use

Pharmacologic properties of commonly used opioids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Analgesia</th>
<th>Sedation</th>
<th>Antitussive</th>
<th>Constipation</th>
<th>Respiratory Depression</th>
<th>Emesis</th>
<th>Physical Dependence</th>
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<tbody>
<tr>
<td>Hydrocodone</td>
<td>+</td>
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<td>0</td>
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<td>0</td>
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<td>Methadone</td>
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<tr>
<td>Methadone</td>
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<tr>
<td>Oxycodone</td>
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<td>Oxycodone</td>
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<td>0</td>
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<tr>
<td>Tylenol w/Codeine #3</td>
<td>APAP 300mg / Codeine 30mg</td>
<td>III</td>
<td>1-2 q4h</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Tylenol w/Codeine #4</td>
<td>APAP 300mg / Codeine 60mg</td>
<td>III</td>
<td>1 q4h</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APAP w/Codeine Elixir</td>
<td>APAP 120mg / Codeine 15mg / 5mL</td>
<td>V</td>
<td>15mL q 4h</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Hydrocodeine
- Viscidin: Hydrocodone 5mg / APAP 300mg
- Norco: Hydrocodone 2.5-10mg / APAP 300mg
- Lortab: Hydrocodone 10mg / APAP 300mg
- Lortab Liquid: Hydrocodone 2.5mg/5mL / APAP 20mg/5mL
- Viconprofen: Hydrocodone 7.5mg / Ibuprofen 200mg

Hydrocodeine 10mg / APAP 300mg
- Schedule: II
- Adult Dose: 1 q 4-6h
**Oxycodone**

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Formulation</th>
<th>Schedule</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percodan</td>
<td>Oxycodone 5mg / Aspirin 325mg</td>
<td>II 1 q 6h</td>
<td>6h 1 q 6h</td>
</tr>
<tr>
<td>Percocet</td>
<td>Oxycodone 2.5-10mg / APAP 325mg</td>
<td>II 1 q 6h</td>
<td>6h 1 q 6h</td>
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<tr>
<td>Roxicodone</td>
<td>Oxycodone 5, 15, 30mg / APAP 325mg</td>
<td>II 1 q 6h</td>
<td>6h 1 q 6h</td>
</tr>
<tr>
<td>Tylox</td>
<td>Oxycodone 5mg / APAP 500mg</td>
<td>II 1 q 6h</td>
<td>6h 1 q 6h</td>
</tr>
</tbody>
</table>

**Tramadol**

- Schedule IV (as of 7/2014)
- 50-100mg q 4-6h
- Not to exceed 400mg/d
- Moderate to moderately severe pain
- Good alternative to patients who cannot tolerate NSAIDs
- No effects on cardiac disease and peptic ulcer disease
- Preg C

- Ultracet (Tramadol + APAP)
- 37.5mg Tramadol/325mg APAP
- Very low action on opioid receptors - ok for abusers?

**Opioid prescribing contraindications**

- Hypersensitivity to any narcotic
- Acute bronchial asthma
- COPD
- Renal or hepatic dysfunction
- Abuse potential

**Opioids and Pregnancy**

- Safety of narcotic analgesics during pregnancy has not been established.
- Use only in extremely necessary cases
- Most of the opioid analgesics appear in small quantities in breast milk, but drug effects in nursing infants appear to be insignificant
- If possible, breastfeeding should be deferred for at least 4 to 6 hours after opioid analgesics are taken.

**Advise Patients**

- Drowsiness, dizziness, or blurred vision can occur. Patients should be cautious when driving or performing other tasks requiring alertness.
- Drug-induced nausea, vomiting, or constipation can occur.
- If GI upset occurs, the medication should be taken with food to decrease GI irritation.
- Alcohol or other CNS depressants should be avoided because they can exacerbate opioid-induced sedation.
- Breathing difficulty or shortness of breath can occur.

**Naloxone**

- Emergency opioid antagonist
- Intramuscularly or by auto injector


Prescribing of Naloxone

- HB 21 provides that for the treatment of pain related to a traumatic injury with an Injury Severity Score of 9 or greater, the healthcare provider who prescribes a Schedule II controlled substance must concurrently prescribe an emergency opioid antagonist (Florida)
- Currently available in 46 states without a prescription.

Prescription writing for opioids/controlled sub

- Must have DEA License (~$731/3yrs)
- FLORIDA
  - MUST check Prescription Drug Monitoring Program (PDMP) “e-FORCe” before prescribing a controlled substance
- GEORGIA
  - DO NOT NEED to check PDMP if not prescribing for longer than 3 days (GA OKE) 7 days

Mid Level Practitioners

Prescribing ability

- Missouri, Iowa, Nebraska, Kansas, TN
  - Schedule 3, 4N, 4, 5
  - Prescribe, Administer & Dispense
- Oklahoma, Arkansas, Kentucky
  - Schedule 3, 4N, 4, 5
  - Prescribe 2 only for Hydrocodone
  - Prescribe, Administer & Dispense
- Illinois
  - Schedule 2-4, 5
  - Prescribe 2 only for Hydrocodone products
- Indiana
  - Schedule 4
  - Administer and Dispense Tramadol only

Alternative Options

- Pharmaceuticals
  - Concomitant use of NSAID and APAP
  - Promethazine (Phenergan)
  - Ambien (Zolpidem)
  - Valium (Diazepam)
  - Cannabidiol (CBD)

Concomitant use of NSAID and Acetaminophen

- A randomized, double-blind, placebo-controlled trial comparing the efficacy and tolerability of analgesic combinations including a novel single-habit combination of Butprofen/Paracetamol for postoperative dental pain
- A novel single-habit combination of Butprofen/Paracetamol for postoperative dental pain
- Values represent a summary of a Phase 2 study in the USA
- Mean±SD; N=253

- 400mg Butprofen/1000mg acetaminophen = 400mg APAP/300mg codeine
- ONLY 15% of patients needed “rescue” medication
**Alternative Options**

**Promethazine (Phenergan)**
- Non-selective H1 Anti-histamine
- Antiemetic and sedative effects
- 12.5 mg, 25 mg, 50 mg q4h
- Oral, Suppository (Rectal)
- Cheap!
- Contraindicated in children <2 YO due to respiratory depression

**Ambian (Zolpidem) 5mg @ bedtime**
- Interacts w/ GABA-benzodiazepine receptor complexes
- Schedule V controlled substance
- No Alcohol
  *May cause severe hallucinations

**Valium (Diazepam)**
- 2-10mg @ bedtime (No Alcohol)
- Schedule IV controlled substance
- Binds to benzodiazepine receptors; enhances GABA effects
- Concomitant use with opioids will enhance effects.

**Cannabinol (CBD)**
- Activates G-protein-coupled receptors, cannabinoid 1 (CB1R) and cannabinoid 2 (CB2R)
- CB1R modulates neurotransmitter release (help with pain response)
- CB2R activation is anti-inflammatory
- Peripheral and Central
- 1% THC, 5% CBD, and 1.5% HU-308 effectively reduced the pain response and reduced neutrophil number

**Ocular Surface Environment Modulation**
- Bandage Contact Lens
- Amniotic Membrane
Ocular Surface Environment Modulation

Bandage Contact Lens

- Off-label therapeutic use of soft contact lens
- Many indications
- 86% success rate achieved - therapeutic goal was pain relief
- K erosion, bullous keratopathy, corneal edema, corneal dystrophy and post-Sx
- Customary dosage and instillation of ocular pharmaceuticals should not be changed.

FDA approved lenses for therapeutic use:
- Acuvue Oasys (Vistakon)
- PureVision (Bausch & Lomb)
- Air Optix N&D (Alcon)
- SoftForm 55 EW (Unilens)

References:

Ocular Surface Environment Modulation

Amniotic Membrane

- Avascular fetal membrane that lies deep to the chorion and is harvested in a sterile environment from placental tissue.

- Benefits:
  - Act as physical barrier for protection
  - Reduces pain
  - Basement membrane promotes epithelial growth
  - Inhibits fibroblast growth and reduces inflammation and scarring potential

- Cryopreserved
  - i.e. Prokera (BioTissue)
  - Stored in freezer
  - No assembly, inserted similar to a contact lens
- Dehydrated
  - i.e. AmbioDisk (IOP Ophthalmics)
  - Kept at room temp – must be rehydrated
  - Applied to ocular surface then covered with an overlying bandage contact lens.

References:

If we are to address pain, we must manage pain.

- Consider all options which may benefit the patient.
- Remember, if it wasn’t painful they wouldn’t be here.

THANK YOU
CONTACT ME

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